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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,790	DAHIYAT ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/19/03*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1 and 10-18 are pending.

Claims 2-9 have been cancelled.

Claims 10-18 are withdrawn from consideration.

Claim 1 is under examination.

Claim Rejections - 35 USC § 101

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility for reasons set forth in the last Office action, 9/26/03.

Response to Arguments

Applicants present several references e.g., U.S. Patent 6,627,186 and journal articles as evidences to support that the instant method has specific and well-established utility.

In response, a review of these references e.g., U.S. 6,627,186 reveals claims to specific compounds, which obviously has a utility. This cannot provide for support for the instant secondary library of undefined constitution or structures. Likewise, the article by Degrado relates to the specific compound, Zinc finger protein or human growth hormone by

Filikov. At the time of applicants' filing, all of the methods relates to a known or particular protein and improvements of the known (parent) protein to create variants with improved properties.

Applicants argue that the claimed method generates virtual libraries of protein sequences that are vastly larger than traditional experimental libraries. By limiting the number of randomized positions and the number of possibilities at these positions, the number of wasted sequences produced in the experimental library is reduced. Applicants further argue by computationally screening large libraries, greater diversity or protein sequences may be screened.

In response, much of applicants' arguments are drawn generally to what advantages or benefits could be derived in using computational method to generate the libraries. It is not apparent from the arguments as to the specific and substantial utility of the libraries generated by the method. Likewise, the computational method of generating diverse and smaller libraries is not a specific and substantial utility. *In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to

play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of **possible use so general as to be meaningless** and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.') (Emphasis ours).

Thus, the secondary library of as yet undefined structure allegedly generated from the claimed method does not have a real-world utility i.e., a specific and substantial or well-established utility.

Claim 1 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes protein design using specific (computational) program design, does not reasonably provide enablement for any type of secondary library of scaffold protein variants or sequences because of the reasons advanced in the last Office action.

Response to Arguments

Applicants argue the present invention utilize well-established protein design methods, founded on basic principles of chemistry e.g., utilizes structural and biophysical knowledge of protein. In response, applicants' argument is contradictory to the claimed method which does not recite for any structure of the protein. It would appear that the vast numbers of proteins would make it nearly impossible to predict from a single protein structure and/or biophysical properties its applicability to the numerous structurally and biophysically different proteins. Applicants argue that the instant method is

not a randomly generated library but a rational design technique, citing page 1, lines 11-25 of the instant specification.

Applicants' argument is unclear. The cited relevant section relates to Protein Design Automation (PDA). It is unclear whether this is what the argument is referring to. If so, the claims do not recite for said PDA. Rather, only computational method which as applicants recognize covers a multitude of method including the shot in the dark, genetic approach. See further applicants' arguments at presumably page 3 (the pages are not numbered), first incomplete paragraph. Further, applicants' attention is drawn to the DeGrado reference newly cited by applicants. Degrado at page 80 states "de novo design is best approached by simultaneously considering all of the side chains in the protein—unfortunately, a very high order combinatorial problem. The enabling disclosure for an enzyme (which covers a broad scope of enzymes) using for the computational method, PDA, would not be enabling for any type of other proteins generated by the broad method steps.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Response to Arguments

In view of applicants' arguments the rejection has been overcome.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 are rejected under 35 U.S.C. 102(b) as being anticipated by Fechteler et al (JMB) for reasons advanced in the last Office action.

Response to Arguments

Applicants argue that Fechteler reference is a homology modeling about predicting protein structure in regions of insertions and deletions. The reference is directed to designing a protein model by homology and predicting what structure the sequence would adopt. The reference does not retain the sequence information because they are focused on the backbone structure. Applicants further argue that the present invention may be

distinguished form the cited reference because there is no suggestion or teaching of synthesizing variants of a secondary library. The present invention is not directed to predicting theoretical 3D structures based solely on homology models and does not rely on insertion and deletion regions.

In reply, attention is drawn to page 128, Methods section of the Fechteler reference. It discloses the details of the method. Designing a protein model is the same concept as the instant method of generating a second variant library, albeit, termed differently. While the Fechteler is silent about synthesizing the obtained protein, however, this does not mean that Fechteler does not teach said synthesis. The claimed method recites for said synthesizing term. The specification however, like Fechteler describes only the computational method of PDA. Not a single compound has been synthesized in the specification, let alone a library. Accordingly, the specific method steps of Fechteler using specific components in the detailed Methods fully meet the broad steps of the claimed method of undefined structure.

Double Patenting

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,403,312.

In view of the terminal disclaimer of record, this rejection no longer applies.

Claim 1 is not allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D.

Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
April 16, 2004